REMARKS

Status of the Claims

Claims 1, 25, 38, 43, 44, 48, 53 and 54 have been amended. Support for the amendments can be found throughout the present specification, for example, see page 17, lines 21-25 of the application as filed. Claims 12-24 and 58 have been cancelled without prejudice or disclaimer. No new matter has been added.

In the Office Action, claims 1-42 and 53-59 were indicated to be withdrawn, and claims 43-52 and 60-63 to be presently under examination.

Applicants note with appreciation the Examiner's withdrawal of the previous rejections under 35 U.S.C. §103(a) (see below).

Rejection of claims under 35 USC 112, first paragraph

In the Office Action, claims 43-52 and 60-63 stand rejected under 35 USC 112, first paragraph, as allegedly lacking enablement. This rejection is traversed.

In the Office Action, at the top of page 4, the Examiner asserts that Applicants' specification "does not reasonably provide enablement for inhibition of tolerance to all narcotic analgesics with all VR1 antagonists" (emphasis in original). Applicants cannot agree.

With regard to "tolerance to all narcotic analgesics," in the Office Action, the Examiner states that "it is understood that common treatments for narcotic analgesic dependence are applicable for all opioids ...[but] ... it is undetermined that the same idea can be extrapolated to non-opioid compounds." Applicants thank the Examiner for this helpful clarification. Without agreeing with the Examiner's position, in the present amendments, independent claims 1, 25, 38, 43, 48 and 53 (and the remaining claims which depend therefrom) are amended to provide that the "narcotic analgesic" is an "opioid narcotic analgesic". Applicants contend that this language is fully enabled by the present specification.

With regard to "inhibition of tolerance ... with all VR1 antagonists," in the Office Action, the Examiner says in discussing the *Wands* factors that the "skilled artisan

would view the inhibition of addiction ... with all VR1 antagonists is highly unlikely" (emphasis in original).

Applicants respectfully disagree. Applicants' specification provides working examples demonstrating that at least three VR1 antagonists (not two as stated in the Office Action) prevent tolerance to repeated opioid dosing and/or reduce side effects due to opioid treatment. As provided in the MPEP, "even in unpredictable arts, a disclosure of every operable species is not required." MPEP 2164.03. All that is required is that one of ordinary skill in the art be able to practice the claimed invention without undue experimentation.

In this case, Applicants have provided ample teachings, including working examples, to permit one of ordinary skill in the art to practice the claimed methods without undue experimentation.

Furthermore, a patent application filed shortly after Applicants' priority date confirms that those of skill in the art expected, after Applicants' priority date, that other VR1 antagonists would function to treat or prevent tolerance to morphine. The application is now Kyle et al., US 6,974,818, currently cited by the Examiner under 35 USC 102(e). Kyle et al. report in Example 6 that, in experiments using morphine, their thiadiazolylpiperazine compounds (described in 6,974,818 as VR1 inhibitors) decrease self administration of morphine (an opioid). In fact, in making the pending 102(e) rejections, the Examiner states in the Office Action that Kyle et al.'s "Example 6 outlines a study proving that the compounds of the Kyle et al. invention are capable of decreasing morphine self-administration (thereby inhibiting tolerance), which is a model for an addictive disorder." Given Applicants' examples of three VR1 antagonists working to prevent tolerance to morphine (in Example 12 of their specification) and the (later) disclosure of the Kyle et al. 6,974,818 patent, that the Kyle thiadiazolylpiperazine compounds (which are chemically distinct from the VR1 antagonists disclosed in Applicants' specification) are also effective in this regard, the Examiner has shown no evidence as to why one of ordinary skill would expect that other VR1 antagonists would not also work.

Therefore, Applicants believe it is established that the skilled artisan would not find a method for the inhibition of addiction of opioid narcotic analgesics with VR1 antagonists "highly unlikely."

In view of all of the above, Applicants respectfully submit that the pending claims fully comply with the requirements of 35 U.S.C. §112.

Rejection of claims under 35 USC 102(e)

In the Office Action, claims 43-45 and 48-50 again stand rejected under 35 U.S.C. §102(e), as allegedly anticipated by Kyle et al., U.S. Patent No. 6,974,818 (the "Kyle patent"). This rejection is traversed.

Without agreeing that the disclosure of the Kyle patent would anticipate or render obvious any of the claims of the instant application, Applicants contend that the Kyle patent is not an effective reference against the claims presently under examination.

As discussed in the previous response (filed August 10, 2007), the disclosure of the Kyle patent is not available for citation under 102(e) unless such disclosure also appears in one of the Kyle patent's priority provisional applications. The Examiner now asserts that in the Kyle patent's priority application 60/411,084 "it is taught that the compounds of the [Kyle] invention are used for the treatment of addictive disorders." The disclosure in that priority application regarding addictive disorders is limited to the lines cited by the Examiner (page 20, lines 15 and 20), which merely recite that compounds disclosed therein "are useful for treating or preventing ... an addictive disorder."

In fact, contrary to the assertion in the Office Action, the cited portion of the Kyle priority application does not teach that VR1 antagonists in general are useful in the treatment of addictive disorders. Instead, the Kyle priority application discloses – at page 20, lines 15 – 20 - that "[e]xamples of conditions that are treatable or preventable by inhibiting mGluR1 function include, but are not limited to . . . pain, UI, an addictive disorder . . . [a]ccordingly, the Thiadiazolepiperazine Compounds are useful for treating or preventing pain, UI, an addictive disorder . . . " (emphasis added).

In contrast, the Kyle priority application states (at page 19, lines 21-22) that the thiadiazolylpiperazine compounds disclosed therein are believed to be VR1

antagonists, and (at page 19, lines 23-31) that methods for inhibiting VR1 function in a cell can be used to "treat[ ] or prevent[ ] . . . pain, urinary incontinence (UI), an ulcer, inflammatory-bowel disease (IBD), and irritable-bowel syndrome (IBS)." Applicants note that the Kyle priority application does not state that VR1 antagonists generally can be used for treatment of addictive disorders (or, more particularly, that VR1 antagonists in general are useful for inhibiting the development of tolerance to a narcotic analgesic in a patient, or for inhibiting the development of dependence on a narcotic analgesic in a patient, as recited by claims 43, 48, and their respective dependent claims). At most, the teachings of Kyle would be limited to the compounds disclosed therein.

Moreover, Applicants point out that the bare recitation of "an addictive disorder" in the Kyle priority application can hardly be said to describe or enable methods for inhibiting the development of tolerance to or dependence on a narcotic analgesic, as recited in the pending claims under examination.

To the extent that the Kyle priority application does mention "that the compounds of the [Kyle] invention are used for the treatment of addictive disorders," as stated in the Office Action, Applicants submit that the Kyle priority application does not enable such use.

MPEP 706.02 (f)(1) I (B) states in part: "The 35 U.S.C. 102(e) date of a reference that did not result from, nor claimed the benefit of, an international application is its earliest effective U.S. filing date, taking into consideration any proper benefit claims to prior U.S. applications under 35 U.S.C. 119(e) or 120 **if** the prior application(s) properly supports the subject matter used to make the rejection in compliance with 35 U.S.C. 112, first paragraph" (emphasis added). Notably, in Kyle's 60/411,084 priority application there is not the slightest enablement provided for using any compound "for treating or preventing ... an addictive disorder" nor is there any disclosure at all (the ultimate in non-enablement) of most of the critical added citations from the Kyle patent 6,974,818 used in the Office Action in making the pending 102(e) rejections.

In particular, the Office Action cites the following portions of the Kyle patent 6,974,818:

- column 12, lines 19-22, which reads:

  "The invention still further relates to methods for inhibiting Vanilloid

Receptor 1 ("VR1 ") function in a cell, comprising contacting a cell capable of expressing VR1 with an effective amount of a Thiadiazolylpiperazine Compound."

- column 5, lines 19-30, which reads:

  "Many drugs can cause physical and/or psychological addiction. Those most well known types of these drugs include opiates, such as heroin, opium, and morphine; sympathomimetics, including cocaine and amphetamines; sedative hypnotics, including alcohol, benzodiazepines and barbiturates; and nicotine, which has effects similar to opioids and sympathomimetics. Drug addiction is characterized by a craving or compulsion for taking the drug and an inability to limit its intake. Additionally, drug dependence is associated with drug tolerance, the loss of effect of the drug following repeated administration, and withdrawal, the appearance of physical and behavioral symptoms when the drug is not consumed."

- column 31, lines 18-25, which reads:

  "Thiadiazolylpiperazine Compounds can be used to treat or prevent an addictive disorder, including but not limited to, an eating disorder, an impulse-control disorder, an alcohol-related disorder, a nicotine-related disorder, an amphetamine-related disorder, a cannabis-related disorder, a cocaine-related disorder, an hallucinogen-related disorder, an inhalant-related disorders, and an opioid-related disorder, all of which are further sub-classified as listed below." and

- column 33, line 32, which reads:

  "Opioid-related disorders include, but are not limited to,".

Of these cited disclosures in the Kyle patent 6,974,818, only the first (which merely discloses that Kyle's thiadiazolylpiperazine compounds can be used to inhibit VR1 function) is arguably supported by the disclosure of Kyle's 60/411,084 priority application. As mentioned above, the disclosure in the Kyle patent (at column 31, line 18) that "[t]hiadiazolepiperazine Compounds can be used to treat or prevent an addictive disorder" does not find enabling support in the Kyle priority application; certainly, the language of the Kyle patent relating to "an opioid-related [addictive] disorder" (column 31, lines 24-25) is not found in the Kyle priority application. Thus, these other cited disclosures of the Kyle patent (6,974,818) are simply not available to

be used to reject the present claims pursuant to 35 U.S.C. §102(e), and the pending §102(e) rejection is completely untenable without them.

Reconsideration and withdrawal of the rejection is proper and the same is requested.

Rejection of claims under 35 U.S.C. §103(a)

In the Office Action (at pages 7-8), claims 46-47, 51-52, and 62-63 stand rejected under 35 U.S.C. §103(a), as allegedly unpatentable over Kyle et al., U.S. Patent No. 6,974,818, in view of Bakthavatchalam et al., U.S. Patent No. 7,074,799 (the "Bakthavatchalam patent"). This rejection is traversed.

As noted above, the Examiner has indicated (at page 3 of the Office Action) that the previous rejection under 35 U.S.C. §103(a) has been withdrawn. Applicants therefore consider that the recitation (at pages 7-8 of the Office Action) of a rejection under 35 U.S.C. §103(a) is simply an error and that this rejection is no longer applied to the subject claims.

However, to ensure a complete response, Applicants reiterate that the Bakthavatchalam patent cannot be used in a rejection under 35 U.S.C. 103(a), as the Examiner concedes at page 3 of the Office Action, and that the rejection over the Kyle patent in view of the Bakthavatchalam patent is therefore improper and should be withdrawn.

Reconsideration and withdrawal of the rejection is proper and the same is requested.

CONCLUSION

For at least the foregoing reasons, Applicants contend that the rejections of record should be withdrawn, and that the present application is in condition for allowance. Early and favorable consideration of the application is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper

hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 60004 (72021).

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Respectfully submitted,

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